



An Overview and Analysis of the Societal Impacts of Taxol Biosynthesis in the United States

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Taxol and cancer treatment:

With a place on the World Health Organization's Model List of Essential Medicines¹, Taxol is undeniably indispensable in treating cancer. Because of its demanding production process, Taxol is expensive and in short supply. Resultantly, access is decreased for people nationally and globally because of limitations based on treatment primarily stemming from high costs, inaccessibility. With the optimization of Taxol biosynthesis, Taxol would become much simpler and cheaper to produce, and would be available in greater quantity and ostensibly at a decreased price. The immediate societal and economic impacts beyond this decrease in production cost are much more nebulous, with cost and accessibility remaining major barriers to cancer treatment in the United States.

The American Cancer Society estimates that in 2016, Americans will be diagnosed with 249,260 new cases of breast cancer, 53,070 new cases of pancreatic cancer, 22,280 new cases of ovarian cancer and 186,244 cases of non-small cell lung cancer and 1,913 cases of Kaposi Sarcoma. As a cytotoxic drug which kills cancer cells, Taxol is used primarily to treat all of these cancers, and is currently in clinical trials for treatment of ovarian, peritoneal and fallopian cancers², as well as potential usage in combination with other cancer drugs in order to tackle particularly difficult cases of drug resistance in deep tissue.

Taxol was initially derived from the bark of the Pacific Yew tree, *Taxus brevifolia*. This was neither a sustainable nor cost-effective endeavour, resulting in limited Taxol production and a negative environmental impact due to the resulting deforestation necessitated by Taxol production. Initial production of Taxol in the 1990's required 20,000 pounds of bark from the Pacific Yew tree, approximately 2000-4000 trees, to produce one kilogram of Taxol³. The limitation in supply prompted a "taxol supply crisis" and a call by the National Cancer Institute

to pursue alternative means of more efficient production⁴. In order to address this shortage, researchers have pursued chemical and semi-chemical synthesis⁵ as well as plant cell fermentation⁶, with current efforts focused on optimizing bacterial biosynthesis. If these efforts prove successful, they will result in a decrease in production cost which could potentially affect treatment cost.

Financial obstacles to cancer treatment:

One of the primary obstacles to cancer treatment continues to be cost. According to a study by the American Economic Association conducted in 2015, the cost of anticancer drugs increased by 10% annually from 1995-2013, which equates to an average launch price of \$8,500/year⁷. This trend allows anticancer manufacturers to set the prices of new produces at or above the prices of existing therapies. Thus, even when cost-effective innovations with regards to synthesis and delivery occur, this does not immediately reflect a decrease in prices, because of the peculiarities of the current anticancer drug market within the United States. Although much of the costliness of anticancer drugs stems from the cost of research and development needed to create a marketable product, the cost of development is often hyper-inflated by advocates for high anticancer drug prices. In an independent analysis, Light and Warburton of Stanford University and the University of Victoria estimate that, contrary to sums of over \$1 billion often cited for the research and development of new drugs, research and development costs a median of only \$43.4 million per new anticancer drug, undermining one of the primary arguments of corporations regarding high anticancer treatment prices⁸.

The anticancer drug market operates in the United States with individual treatment agents creating a monopoly because of the nature of the progression of cancer as a disease. Because

cancer is not easily curable and often requires several different methods and forms of delivery to be targeted and treated, several different kinds of drugs and treatments are often used simultaneously. This means that the entrance of new drugs within the market do not necessarily push other drugs out because they have different uses and are often used in tandem. Furthermore, when the same drug is improved (as in the case of the optimized biosynthesis of Taxol), the older version of the drug is viewed as outdated and not as effective, so the newest version of the drug is priced at a higher level, even if it is produced in a more cost-effective manner. Finally, people are willing to accept higher prices for anticancer treatment because of the often incurable and extremely serious nature of a cancer diagnosis. With no alternative in terms of cost or quality, people must simply acquiesce to extremely high prices in return for treatment⁹.

Although the recent Affordable Care Act enacted by President Barack Obama in 2012 has expanded coverage for over 16.4 million people as of 2015¹⁰, the cost of Taxol treatment, even with insurance, is considerable given the median annual income within the United States which stands as of 2015 at \$56,516¹¹. Taxol treatments without insurance amount to approximately \$3076 per treatment¹², or \$439.39 with Medicaid¹³. With Taxol treatments typically administered once every two weeks, this amounts to approximately \$80,000 without insurance, far surpassing the median annual income of an American family and \$11,420 with Medicaid, still a sizeable amount of income, for one year of treatment,. These numbers only take into account the payment for treatment itself, and do not take into account the additional cost for visiting oncologists or additional equipment needed for the treatment. Furthermore, as cancer treatments are extremely variable and many are long-term, for many individuals Taxol treatments would continue beyond one year and would be coupled with other, more expensive anticancer drugs.


We must also continue to consider the 8.6% Americans who remain uninsured within the United States¹⁴. The majority of these individuals work full time jobs but are unable to be insured because of the cost of insurance even after it has decreased considerably under the Affordable Care Act, and are ineligible for Medicare and Medicaid¹⁵. 38% of the uninsured population within the United States lives below the poverty level in the United States which currently is defined by earning \$24,300 for a family of four¹⁶. Although some of these individuals are targeted by Medicare, there remain significant obstacles to eligibility those who remain uninsured would be entirely unable to pay the \$80,000 required for a yearly Paxitacel treatment for breast cancer, which must be continued until the cancer goes into remission or progresses into a further stage, without falling deeply into debt. Further compounding the situation is the fact that minorities within the United States are uninsured at a greater rate than White individuals, with one-third of Hispanics and one-fifth of black Americans currently uninsured within the United States¹⁷.

Individuals without healthcare have also been demonstrated to have poorer health as a whole than their counterparts who have a health insurance plan¹⁸. A large part of this stems from the exorbitant prices of medical care within the United States without health insurance (as demonstrated by the \$80,000/year price tag of Taxol treatment). Individuals with health concerns and no health insurance will understandably put off seeing doctors for chronic and sudden health concerns until their health condition worsens and becomes unavoidable, by which point treatment is no longer preventative. By this time, their ailments have progressed to a stage where treatment is far more difficult and expensive, but the individuals still do not have health insurance to support them.

Access-related obstacles to cancer treatment:

In addition to the cost barrier, access is yet another obstacle to increasing the population receiving cancer treatments. Taxol is most frequently administered in high doses once every two weeks. Recently, however, professionals have advocated for weekly dosages in less concentrated amounts for the treatment of breast cancer, for a dose which is less concentrated and equally effective, minimizing the frequency of neurologic toxicity common with the bi-weekly schedule¹⁹. In order for treatment to be effective, patients must receive the treatments on a set schedule regulated by physicians depending on what is necessitated for their specific type of cancer. However, the simple act of going to a hospital or healthcare provider in order to receive treatment is a luxury not afforded to many Americans. Individuals living in urban, rural and suburban areas all face issues of accessibility, many of which stem from underlying financial burdens. In addition to footing the exorbitant bill of anticancer treatment, patients are responsible for seeking out and transporting themselves to a healthcare provider which is capable of administering the anticancer treatment.

Transportation becomes an immediate issue, as the 59,429,276 individuals living in rural areas within the United States²⁰ will not live within the immediate vicinity of a hospital or properly equipped healthcare provider, and will have to travel up to several hours in order to visit an oncologist. Individuals in suburban and urban areas face similar obstacles although not to such an extreme extent, as if they do not own vehicles they are often unable to travel to an oncologist unless there is an existing system of reliable and regular public transportation, a detail which is extremely variable even within different neighbourhoods of the same city. On that same note, elderly individuals or individuals with other chronic conditions or stages of advanced



cancer often lack the independence to transport themselves to an oncologist, and therefore are unable to benefit from decreases in treatment costs.

Continuing with the issue of access, because of the regularity of Taxol treatments, which have been further encouraged by professionals to increase in frequency, cancer patients are constrained by their oncologists regarding treatment times. Patients who remain in the workforce during their cancer treatments will potentially miss work in order to make regular treatments and ensure the most effective delivery of Taxol. Given the highly variable length of time needed for cancer treatment, stricter work environments will not tolerate such absenteeism even for serious health concerns. Patients will then have to choose between effective anticancer treatments or a steady job. Healthcare is often supplied by employers, and if people become unemployed due to missing work because of anticancer treatments, they will lose their healthcare coverage and source of income, making it doubly difficult to afford cancer treatments regardless of price decreases.

Policy recommendations:

In planning for an ideal societal impact once Taxol is optimally biosynthesized and production costs are lower, policymakers and scientists alike must take into account the unique dynamics of the anticancer drug market within the United States. Taxol must be marketed to be competitive with other more expensive taxenes and cytotoxic drugs, and at a price which is considerably less than the estimated current \$439.39 per treatment with insurance, so as to be more reasonably priced for individuals with and without insurance plans. Further research must also be conducted regarding the optimization of treatment frequency, as less frequent but equally effective treatments are ideal for individuals in the workforce who resultantly do not have to take

as many extended absences from work. At a more systemic level, local, state and federal governments need to address accessibility to healthcare services by instituting low-cost or free transportation services for individuals living in areas without reliable access to public transportation, and strategically increasing the number of oncologists and general healthcare services available in rural areas. Finally, although the Affordable Care Act has increased insurance coverage within the United States, minorities remain particularly vulnerable as they are uninsured at a greater rate than White Americans, an issue which needs to be addressed by re-evaluating exemptions to Medicare and Medicaid, creating multi-lingual health insurance information and sign-up materials, and re-evaluating both policies by employment agencies regarding health insurance plans as well as health care plan pricing as a whole to reflect the assorted economic realities of American citizens.

The two primary issues of cost and access which cancer patients in the United States currently face regarding anticancer treatment unfortunately are not resolved by the reduction of production costs through the optimized biosynthesis of Taxol. The current anticancer drug market supports high prices. Even with the introduction of cheaper options in the form of generic or older forms of the drugs, patients are encouraged to use the newest (and usually most expensive) form of the drug in their treatment. Furthermore, because of the nature of cancer treatment, drugs are often used in combination and simultaneously, so the decrease of one drug will not necessarily mean a significant decrease in the overall cost of the treatment. When these issues are coupled with the obstacles to accessibility to healthcare services overall, it becomes clear that the cost reduction of Taxol through biosynthesis must still face multidimensional societal and economic issues before profoundly impacting cancer patients through decreases in treatment cost and expansion of access.

Endnotes:

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